1651

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CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper (along with any paper referred to as being transmitted therewith) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

Tina Dasco
(Print Name)

Date: 12-21-99 (Signature)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of: Gelfand et al.

Docket No.: 8636

Serial No.:07/873,897

Group Art Unit: 1651

Filed: April 24, 1992

Examiner: D. Naff

For: PURIFIED THERMOSTABLE ENZYME

COMMUNICATION

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

The present application[1] is a second-generation descendent of a continuation-in-part application of application Serial No. 07/069,509, filed June 17, 1987, which issued as United States Patent No. 4,889,818 (the "'818 patent"). The '818 patent has been in litigation[2], and the Court on December 7, 1999, handed down a decision after a trial on inequitable conduct which took place in February, 1999. Applicants have submitted the Court's decision in the Third Supplemental Information Disclosure Statement, dated December 20, 1999.

[1] The present application is a file wrapper continuation of application Serial No. 07/387,003, filed July 28, 1989, which is a divisional of application Serial No. 07/143,441, filed January 12, 1988, which is a continuation-in-part of application Serial No., 07/063,509, filed June 17, 1987, which issued as the '818 patent.

[2] The litigation is currently pending in the Northern District of California, Hoffmann-LaRoche Inc. and Roche Molecular Systems, Inc. v. Promega Corporation, Civil Action No. C-93-1748 VRW.

Applicants note that errors in Figures 1 and 2 of the '818 patent were pointed out during the litigation. However, the Court did not find that the presence of errors in the figures was evidence of inequitable conduct.

Figures 2 and 3 of the present application are the same figures as Figures 1 and 2 of the '818 patent and, thus, contain the same errors. Applicants believe that the errors in Figures 2 and 3 are not relevant to the patentability of the pending claims, now allowed, in the present case. However, in the public interest, Applicants wish to note for the record the errors in the Figures 2 and 3 of the present application, and to indicate the corrections.

Figure 2 is a restriction site map of plasmid pFC83 that contains the ~4.5 kb HindIII *Thermus aquaticus* (Taq) DNA insert subcloned into plasmid BSM13+. Plasmid pFC83 was deposited with the American Type Culture Collection on May 29, 1987, and is available as ATCC 67,422.

Figure 3 is a restriction site map of plasmid pFC85 that contains the ~2.68 kb HindIII to Asp718 Taq DNA insert subcloned into plasmid BSM13+. Plasmid pFC85 was deposited with the American Type Culture Collection on May 29, 1987, and is available as ATCC 67,421.

As described in the specification at page 12, lines 16-26, the gene encoding Taq DNA polymerase can be constructed by ligating an ~730 base pair (bp) BglII-HindIII restriction fragment isolated from plasmid pFC83 to an ~2.68 kilobase pair (kb) HindIII-Asp718 restriction fragment isolated from plasmid pFC85. The restriction fragment from pFC83 comprises that portion of the Taq DNA polymerase gene which encodes the amino-terminal portion of the enzyme, and the restriction fragment from pFC85 comprises that portion of the gene which encodes the carboxy-terminal portion of the enzyme.

The entire gene sequence that encodes Taq DNA polymerase is provided in Figure 1 of the specification. The location of restriction sites within the sequence of Figure 1 can be ascertained routinely by a simple inspection of the sequence. Thus, the sequence provided in Figure 1 provides the correct locations of the restriction sites within those portions of the restriction maps shown in Figures 2 and 3 which correspond to the Taq DNA polymerase gene.

Figure 2

As noted above, the ~730 bp BglII-HindIII fragment at the right side of the 4.5 kb insert shown in Figure 2 corresponds to the portion of the gene that encodes the amino-terminal portion of the enzyme. The locations of the restriction sites in the corresponding portion of Figure 1 are listed below. The sites, with the exception of the BssHII site (marked with an asterisk) are explicitly indicated in Figure 1. The location of the BssHII site is apparent from an inspection of Figure 1.

Restriction Enzyme	Sequence	Position in DNA Sequence of Figure 1
BglII	AGATCT	-114 - -109
BssHII*	GCGCGC	325 - 330
XhoI	CTCGAG	331 - 336
HindIII	AAGCTT	616 - 621

Based on the locations of the restriction sites within Figure 1 listed above, it is apparent that the restriction map in Figure 2 correctly is as indicated below:

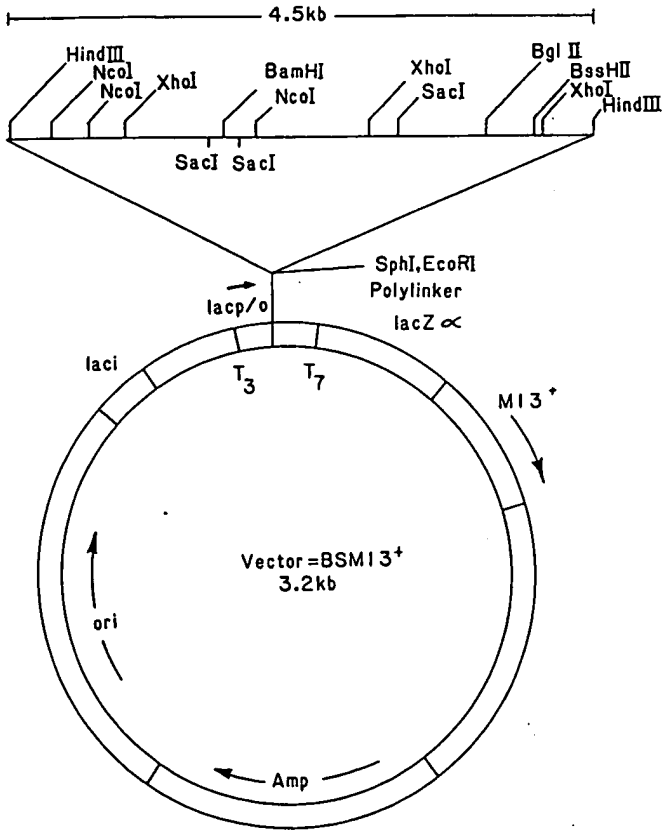

FIG.2

Figure 3

As noted above, the ~2.68 kb HindIII-Asp718 restriction fragment contains the sequence the encodes the carboxy-terminal portion of the enzyme. The locations of the restriction sites in the corresponding portion of Figure 1 are indicated below. Also shown is the location of the stop codon indicating the end of the protein coding region. The sites, with the exception of the SmaI sites (marked with asterisks), are explicitly indicated in Figure 1. The SmaI sites are apparent from an inspection of Figure 1.

Restriction Enzyme	Sequence	Position in DNA Sequence of Figure 1
XhoI	CTCGAG	1408 - 1413
SmaI*	CCCGGG	1457 - 1462
PvuII	CAGCTG	1465 - 1470
PstI	CTGCAG	1597 - 1602
SacI	GAGCTC	1609 - 1614
BamHI	GGATCC	1778 - 1783
SacI	GAGCTC	1843 - 1848
PvuII	CAGCTG	1929 - 1934
SmaI*	CCCGGG	1949 - 1954
NheI	GCTAGC	2043 - 2048
SmaI*	CCCGGG	2204 - 2209
XhoI	CTCGAG	2365 - 2370
Stop Codon	TGA	2497 - 2499

Based on the locations of the restriction sites within Figure 1 listed above, the correct restriction map in Figure 3 within the region corresponding to the sequence in Figure 1 is apparent. In addition to those errors in Figure 3 which are readily apparent from Figure 1, Applicants are aware of additional errors in the restriction map of Figure 3 that lie outside the region corresponding to Figure 1 (i.e., the right-most portion in Figure 3). These errors would be identified and the correct restriction map made apparent by routine sequencing of the insert of plasmid pFC85, which was deposited with the ATCC (see above). Thus, the correct DNA sequence and correct restriction map were provided inherently with the deposit of plasmid pFC85.

Based on the locations of the restriction sites within Figure 1 listed above and the locations which are made apparent by routine sequencing of plasmid pFC85, it is apparent that the restriction map in Figure 3 correctly is as indicated below:

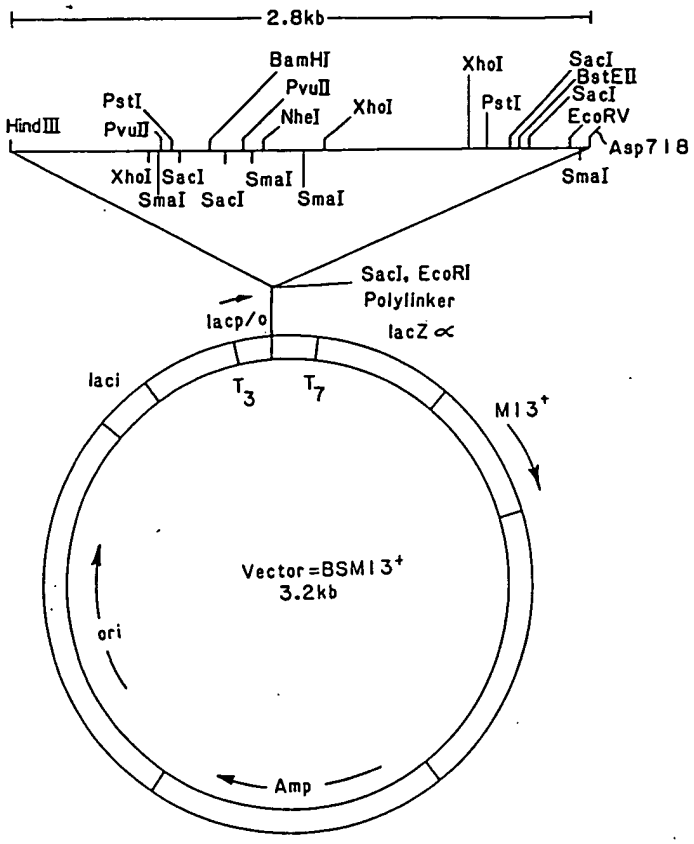

FIG.3

Finally, Applicants note that the size of the insert in Figure 3 is closer to 2.7kb, based on the size (~2.68 kb) indicated in the specification at page 12 (see above).

Respectfully submitted,

Date: December 21, 1999

35,321
(Reg. No.)

Douglas A. Petry, Ph.D.
1145 Atlantic Avenue
Alameda, CA 94501
Telephone (510) 814-2974
Telefax (510) 814-2973

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TRANSMITTAL SHEET

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicants herewith submit the accompanying Third Supplemental Information Disclosure Statement Under 37 C.F.R. § 1.56 and § 1.97, List of References Cited by Applicant, and Petition For Consideration Of Information Disclosure Statement Under 37 C.F.R. § 1.97(d)(2). Applicants request that these papers be entered into the record.

The fee required to be filed in connection with the accompanying Petition For Consideration Of Information Disclosure Statement Under 37 C.F.R. § 1.97(d)(2) for the

above-identified application, pursuant to 37 C.F.R. § 1.17(i), has been estimated to be $130.00. Please charge the required fee to Deposit Account Number 500812. A duplicate of this sheet is enclosed for accounting purposes.

Respectfully submitted,

Date: December 20, 1999

Douglas A. Petry, Ph.D. 35,321 (Reg. No.)
1145 Atlantic Avenue
Alameda, CA 94501
Telephone (510) 814-2974
Telefax (510) 814-2973

Enclosures